

## AMENDMENTS TO THE CLAIMS

Claim 1 (currently amended): A controlled-release Galenical preparation of pharmaceutically acceptable form of Diltiazem including the pharmaceutically acceptable salts thereof, suitable for evening dosing every 24 hours the dosage comprising at least one bead comprising a core and at least one coating, the at least one bead containing from about 120 mg to about 540 mg of the form of Diltiazem, the Diltiazem in the core of the at least one bead associated with excipients, said at least one coating comprising at least one lubricant and/or at least one hydrophilic polymer and at least one water insoluble swellable polymer, whereby the at least one coating permits hydration of the core by gastrointestinal fluids, the coated bead providing to provide controlled (sustained) release of the form of Diltiazem from the preparation for providing a Cmax of Diltiazem in the blood at between about 10 hours and about 15 hours (~~Tmax~~) after administration of the preparation, the preparation being in a sustained-release dosage form in which the form of Diltiazem is adapted to be control released after administration of the preparation over a period of time and being adapted to release the form of Diltiazem

71 (i) into an aqueous medium at the following rates measured using the method of United States Pharmacopoeia No. XXIII at 100 rpm in 900 ml of water:

- (a) between about 1% and about 15% after 2 hours;
- (b) between about 7% and about 35% after 4 hours;
- (c) between about 30% and about 58% after 8 hours;
- (d) between about 55% and about 80% after 14 hours; and
- (e) and in excess of about 75% after 24 hours.

and/or (ii) into a buffered medium having a pH between about 5.5 and about 6.5, at the following rates measured using the method of United States Pharmacopoeia No. XXIII at 100 rpm in 900ml of the buffered medium:

- (a) between about 1% and about 25% after about 2 hours;
- (b) between about 7% and about 45% after about 4 hours;
- (c) between about 30% and about 68% after about 8 hours;
- (d) in excess of about 75% after about 24 hours.

Claim 2 (currently amended): A controlled-release Galenical preparation of pharmaceutically acceptable form of Diltiazem including the pharmaceutically acceptable salts thereof, suitable for evening dosing every 24 hours the dosage comprising at least one bead comprising a core and at least one coating, the at least one bead containing from about 120 mg to about 540 mg of the form of Diltiazem, the Diltiazem in the core of the at least one bead associated with excipients, said at least one coating comprising at least one lubricant and/or at least one hydrophilic polymer, and at least one water insoluble swellable polymer, whereby the at least one coating permits hydration of the core by gastrointestinal fluids, the coated bead

~~providing to provide~~ controlled (sustained) release of the form of Diltiazem from the preparation for providing a C<sub>max</sub> of Diltiazem in the blood at between about 10 hours and about 15 hours (~~T<sub>max</sub>~~) after administration, the preparation being in a sustained-release dosage form in which the form of Diltiazem is adapted to be control released after administration of the preparation over a period of time and being adapted to release the form of Diltiazem

(i) into an aqueous medium at the following rates measured using the method of United States Pharmacopoeia No. XXIII at 100 rpm in 900 ml of water:

- (a) between about 4% and about 8% after 2 hours;
- (b) between about 16% and about 21% after 4 hours;
- (c) between about 44% and about 52% after 8 hours;
- (d) between about 69% and about 76% after 14 hours; and
- (e) and in excess of about 85% after 24 hours;

and/or (ii) into a buffered medium having a pH about 5.8 at the following rates measured using the method of United States Pharmacopoeia No. XXIII at 100 rpm in 900ml of the buffered medium:

- (a) between about 4% and about 15% after 2 hours;
- (b) between about 16% and about 30% after 4 hours;
- (c) between about 44% and about 62% after 8 hours;
- (d) in excess of about 80% after 24 hours.

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Claim 3 (currently amended): The preparation of claim 1 or 2 wherein the lubricant is selected from the group consisting of talc, magnesium stearate and a polyethylene glycol derivative and/or the hydrophilic polymer is selected from the group consisting of hydroxypropylmethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, povidone and any combination thereof ~~C<sub>max</sub> of Diltiazem in the blood is obtained between about 11 - about 13 hours after administration of the preparation.~~

Claim 4 (currently amended): The preparation of claim 2 wherein the C<sub>max</sub> of Diltiazem in the blood is obtained between about 11 - about 13 hours after administration of the preparation.

Claim 5 (previously amended): The preparation of claim 1, 2, 3 or 4 wherein the preparation is a diffusion controlled preparation.

Claim 6 (previously amended): The preparation of claim 1, 2, 3, or 4 wherein the preparation releases the form of Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution.

Claim 7 (previously amended): The preparation of claim 1, 2, 3, or 4 wherein the preparation is in capsule form.

Claim 8 (previously amended): The preparation of claim 1, 2, 3, or 4 wherein the preparation is in tablet form.

Claim 9 (previously amended): The preparation of claim 1, 2, 3, or 4 wherein the preparation comprises a plurality of microgranules, each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises the form of Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent.

Claim 10 (previously amended): The preparation of claim 1, 2, 3 or 4 wherein the preparation comprises a plurality of microgranules, each microgranule comprising a central core containing the form of Diltiazem coated with a microporous membrane and the central core comprises the form of Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the form of Diltiazem is mixed with the wetting agent.

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Claim 11 (previously amended): The preparation of claim 1, 2, 3 or 4 wherein the preparation comprises a plurality of microgranules, each microgranule comprising a central core containing the form of Diltiazem coated with a microporous membrane and the central core comprises the form of Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the form of Diltiazem is mixed with the wetting agent wherein the wetting agent assists to maintain the solubility of the form of Diltiazem in each bead, ensuring that the solubility of the form of Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein.

Claim 12 (previously amended): The preparation of claim 1, 2, 3 or 4 wherein the preparation comprises a plurality of microgranules, each microgranule comprising a central core containing the form of Diltiazem coated with a microporous membrane and the central core comprises the form of Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation.

Claim 13 (currently amended): The preparation of claim 1, 2, 3 or 4 wherein the preparation comprises a plurality of microgranules, each microgranule comprising a central core containing the form of Diltiazem coated with a microporous membrane and the central core comprises the form of Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent wherein the preparation comprises a

mixture of the form of Diltiazem and/or pharmaceutically acceptable salt with the wetting agent and the membrane comprises a water-dispersible or water-soluble polymer and the at least one water insoluble swellable polymer comprises a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation.

Claim 14 (currently amended): The preparation of claim 1, 2, 3 or 4 wherein the preparation comprises a plurality of microgranules, each microgranule comprising a central core containing the form of Diltiazem coated with a microporous membrane and the central core comprises the form of Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent wherein the membrane comprises a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester and hydroxypropylmethylcellulose and the at least one water insoluble swellable polymer comprises a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester.

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Claim 15 (previously amended): The preparation of claim 1, 2, 3 or 4 wherein the preparation comprises a plurality of microgranules, each microgranule comprising a central core containing the form of Diltiazem coated with a microporous membrane and the central core comprises the form of Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent, and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the form of diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside).

Claim 16 (previously amended): The preparation of claim 9 wherein the form of Diltiazem is mixed with the wetting agent and the membrane comprises N,N,N-trimethyl-2-[(2-methyl-1-oxo-2-propenyl)oxy]-chloride ethanaminium polymer with ethyl-2-propenoate and methyl-2-methyl-2-propenoate, an acrylic polymer and plasticizer combined to form the membrane thereby providing a mechanism of release from this membrane which "washes" the form of diltiazem through pores created when the plasticizer incorporated in the membrane, is released in gastrointestinal fluid.

Claim 17 (previously amended): The preparation of claim 1, 2, 3, or 4 wherein the preparation comprises a plurality of microgranules comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises the form of Diltiazem or a pharmaceutically acceptable salt thereof associated with a dissolution agent (other than a wetting agent) to assist in the release of the form of Diltiazem from the preparation.

Claim 18 (previously amended): The preparation of claim 1, 2, 3 or 4 wherein the preparation comprises a plurality of microgranules comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or a pharmaceutically acceptable salt thereof associated with a dissolution agent (other than a wetting agent) to assist in the release of the form of Diltiazem from the preparation and wherein the dissolution agent is an organic acid selected from the group consisting of adipic acid, ascorbic acid, citric acid, fumaric acid, malic acid, succinic acid, tartaric acid which permits the form of diltiazem to dissolve in gastrointestinal fluids when the microgranules pass into the higher pH regions of the gastrointestinal tract of the intestine at which pH diltiazem is much less soluble.

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Claim 19 (currently amended): A method of treatment of a patient's hypertension and/or angina comprising the administration of the preparation of ~~claim 1~~ to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning the preparation comprising a controlled-release Galenical preparation of pharmaceutically acceptable form of Diltiazem selected from the group consisting of Diltiazem and the pharmaceutically acceptable salts thereof, suitable for evening dosing every 24 hours the dosage comprising at least one bead comprising a core and at least one coating, the at least one bead containing from about 120 mg to about 540 mg of the form of Diltiazem, the Diltiazem in the at least one bead associated in the core of each bead with excipients, said at least one coating comprising at least one lubricant and/or at least one hydrophilic polymer and at least one water insoluble swellable polymer, whereby the at least one coating permits hydration of the core by gastrointestinal fluids, the at least one bead providing controlled (sustained) release of the form of Diltiazem for providing a Cmax of Diltiazem in the blood at between about 10 hours and about 15 hours after administration, the preparation comprising the form of Diltiazem in oral sustained-release dosage form in which the form of Diltiazem is adapted to be released after administration over a prolonged period of time and being adapted to release the form of Diltiazem

(i) into an aqueous medium at the following rates measured using the method of United States Pharmacopoeia No. XXIII at 100 rpm in 900 ml of water:

- (a) between about 1% and about 15% after 2 hours;
- (b) between about 7% and about 35% after 4 hours;
- (c) between about 30% and about 58% after 8 hours;
- (d) between about 55% and about 80% after 14 hours; and
- (e) and in excess of about 75% after 24 hours.

and/or (ii) into a buffered medium having a pH between about 5.5 and about 6.5, at the following rates measured using the method of United States Pharmacopoeia No. XXIII at 100 rpm in 900ml of the buffered medium:

- \_\_\_\_\_ (a) between about 1% and about 25% after about 2 hours;
- \_\_\_\_\_ (b) between about 7% and about 45% after about 4 hours;
- \_\_\_\_\_ (c) between about 30% and about 68% after about 8 hours;
- \_\_\_\_\_ (d) in excess of about 75% after about 24 hours

the method comprising administering to a patient in need thereof, the preparation in the evening.

Claim 20 (currently amended): A method of treatment of a patient's hypertension and/or angina comprising the administration of the preparation ~~of claim 2~~ to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning, the preparation comprising a controlled-release Galenical preparation of pharmaceutically acceptable form of Diltiazem selected from the group consisting of Diltiazem and the pharmaceutically acceptable salts thereof, suitable for evening dosing every 24 hours the dosage comprising at least one bead comprising a core and at least one coating, the at least one bead containing from about 120 mg to about 540 mg of the form of Diltiazem, the Diltiazem in the at least one bead associated in the core of each bead with excipients, said at least one coating comprising at least one lubricant and/or at least one hydrophilic polymer, and at least one water insoluble swellable polymer, whereby the at least one coating permits hydration of the core by gastrointestinal fluids, the at least one bead providing controlled (sustained) release of the form of Diltiazem for providing a Cmax of Diltiazem in the blood at between about 10 hours and about 15 hours after administration, the preparation comprising the form of Diltiazem in oral sustained-release dosage form in which the form of Diltiazem is adapted to be released after administration over a prolonged period of time and being adapted to release the form of Diltiazem

(i) into an aqueous medium at the following rates measured using the method of United States Pharmacopoeia No. XXIII at 100 rpm in 900 ml of water:

- \_\_\_\_\_ (a) between about 4% and about 8% after 2 hours;
- \_\_\_\_\_ (b) between about 16% and about 21% after 4 hours;
- \_\_\_\_\_ (c) between about 44% and about 52% after 8 hours;
- \_\_\_\_\_ (d) between about 69% and about 76% after 14 hours; and
- \_\_\_\_\_ (e) and in excess of about 85% after 24 hours;

and/or (ii) into a buffered medium having a pH about 5.8 at the following rates measured using the method of United States Pharmacopoeia No. XXIII at 100 rpm in 900ml of the buffered medium:

- \_\_\_\_\_ (a) between about 4% and about 15% after 2 hours;
- \_\_\_\_\_ (b) between about 16% and about 30% after 4 hours;
- \_\_\_\_\_ (c) between about 44% and about 62% after 8 hours;
- \_\_\_\_\_ (d) in excess of about 80% after 24 hours

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the method comprising administering to a patient in need thereof, the preparation in the evening.

Claim 21 (currently amended): A method of claim 19 or 20 wherein the lubricant is selected from the group consisting of talc, magnesium stearate and a polyethylene glycol derivative and/or the hydrophilic polymer is selected from the group consisting of hydroxypropylmethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, povidone and any combination thereof ~~treatment of a patient's hypertension and/or angina comprising the administration of the preparation of claim 3 to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning.~~

Claim 22 (currently amended): A method of claim 19 wherein the C<sub>max</sub> of Diltiazem in the blood is obtained between about 11 - about 13 hours after administration of the preparation ~~treatment of a patient's hypertension and/or angina comprising the administration of the preparation of claim 4 to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning.~~

Claim 23 (currently amended): A method of claim 20 wherein the preparation is a diffusion controlled preparation ~~treatment of a patient's hypertension and/or angina comprising the administration of the preparation of claim 5 to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning.~~

Claim 24 (currently amended): A method of claim 19, 20, 21, 22 or 23 wherein the preparation releases the form of Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution ~~treatment of a patient's hypertension and/or angina comprising the administration of the preparation of claim 6 to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning.~~

Claim 25 (currently amended): A method of claim 19, 20, 21, 22 or 23 wherein the preparation is in capsule form ~~treatment of a patient's hypertension and/or angina comprising the administration of the preparation of claim 7 to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning.~~

Claim 26 (currently amended): A method of claim 19, 20, 21, 22 or 23 wherein the preparation is in tablet form ~~treatment of a patient's hypertension and/or angina comprising the administration of the preparation of claim 8 to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning.~~

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Claim 27 (currently amended): A method of claim 19, 20, 21, 22 or 23 wherein the preparation comprises a plurality of microgranules, each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises the form of Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent ~~treatment of a patient's hypertension and/or angina comprising the administration of the preparation of claim 9 to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning.~~

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Claim 28 (currently amended): A method of claim 19, 20, 21, 22 or 23 wherein the preparation comprises a plurality of microgranules, each microgranule comprising a central core containing the form of Diltiazem coated with a microporous membrane and the central core comprises the form of Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the form of Diltiazem is mixed with the wetting agent ~~treatment of a patient's hypertension and/or angina comprising the administration of the preparation of claim 10 to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning.~~

Claim 29 (currently amended): A method of claim 19, 20, 21, 22 or 23 wherein the preparation comprises a plurality of microgranules, each microgranule comprising a central core containing the form of Diltiazem coated with a microporous membrane and the central core comprises the form of Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the form of Diltiazem is mixed with the wetting agent wherein the wetting agent assists to maintain the solubility of the form of Diltiazem in each bead, ensuring that the solubility of the form of Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein ~~treatment of a patient's hypertension and/or angina comprising the administration of the preparation of claim 11 to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning.~~

Claim 30 (currently amended): A method of claim 19, 20, 21, 22 or 23 wherein the preparation comprises a plurality of microgranules, each microgranule comprising a central core containing the form of Diltiazem coated with a microporous membrane and the central core comprises the form of Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation ~~treatment of a patient's hypertension and/or angina comprising the administration of the~~



~~preparation of claim 12 to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning.~~

Claim 31 (currently amended): A method of claim 19, 20, 21, 22 or 23 wherein the preparation comprises a plurality of microgranules, each microgranule comprising a central core containing the form of Diltiazem coated with a microporous membrane and the central core comprises the form of Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent wherein the preparation comprises a mixture of the form of Diltiazem and/or pharmaceutically acceptable salt with the wetting agent and the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation ~~treatment of a patient's hypertension and/or angina comprising the administration of the preparation of claim 13 to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning.~~

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Claim 32 (currently amended): A method of claim 19, 20, 21, 22 or 23 wherein the preparation comprises a plurality of microgranules, each microgranule comprising a central core containing the form of Diltiazem coated with a microporous membrane and the central core comprises the form of Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent wherein the water insoluble swellable polymer in the membrane comprises a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester and hydroxypropylmethylcellulose ~~treatment of a patient's hypertension and/or angina comprising the administration of the preparation of claim 14 to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning.~~

Claim 33 (currently amended): A method of claim 19, 20, 21, 22 or 23 wherein the preparation comprises a plurality of microgranules, each microgranule comprising a central core containing the form of Diltiazem coated with a microporous membrane and the central core comprises the form of Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent, and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the form of diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside ~~treatment of a patient's hypertension and/or angina comprising the administration of the preparation of claim 15 to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning.~~

Claim 34 (currently amended): A method of claim 19, 20, 21, 22 or 23 wherein the form of Diltiazem is mixed with the wetting agent and the membrane comprises

N,N,N-trimethyl-2-[(2-methyl-1-oxo-2-propenyl)oxy]-chloride ethanaminium polymer with ethyl-2-propenoate and methyl-2-methyl-2-propenoate, an acrylic polymer and plasticizer combined to form the membrane thereby providing a mechanism of release from this membrane which "washes" the form of diltiazem through pores created when the plasticizer incorporated in the membrane, is released in gastrointestinal fluid treatment of a patient's hypertension and/or angina comprising the administration of the preparation of claim 16 to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning.

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Claim 35 (currently amended): A method of claim 19, 20, 21, 22 or 23 wherein the preparation comprises a plurality of microgranules comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises the form of Diltiazem or a pharmaceutically acceptable salt thereof associated with a dissolution agent (other than a wetting agent) to assist in the release of the form of Diltiazem from the preparation treatment of a patient's hypertension and/or angina comprising the administration of the preparation of claim 17 to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning.

Claim 36 (currently amended): A method of claim 19, 20, 21, 22 or 23 wherein the preparation comprises a plurality of microgranules comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or a pharmaceutically acceptable salt thereof associated with a dissolution agent (other than a wetting agent) to assist in the release of the form of Diltiazem from the preparation and wherein the dissolution agent is an organic acid selected from the group consisting of adipic acid, ascorbic acid, citric acid, fumaric acid, malic acid, succinic acid, tartaric acid which permits the form of diltiazem to dissolve in gastrointestinal fluids when the microgranules pass into the higher pH regions of the gastrointestinal tract of the intestine at which pH diltiazem is much less soluble treatment of a patient's hypertension and/or angina comprising the administration of the preparation of claim 18 to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning.

Claim 37 (previously amended): The preparation of claim 1, 2, 3, or 4 wherein the preparation contains 120 mg of Diltiazem.

Claim 38 (previously amended): The preparation of claim 1, 2, 3, or 4 wherein the preparation contains 180 mg of Diltiazem.

Claim 39 (previously amended): The preparation of claim 1, 2, 3, or 4 wherein the preparation contains 240 mg of Diltiazem.

Claim 40 (previously amended): The preparation of claim 1, 2, 3, or 4 wherein the preparation contains 300 mg of Diltiazem.

Claim 41 (previously amended): The preparation of claim 1, 2, 3, or 4 wherein the preparation contains 360 mg of Diltiazem.

Claim 42 (previously amended): The preparation of claim 1, 2, 3, or 4 wherein the preparation contains 420 mg of Diltiazem.

Claim 43 (previously amended): A method of treatment of a patient's hypertension and/or angina comprising the administration of the preparation of claim 37, 38, 39, 40, 41 or 42 to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning.

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Claim 44 (currently amended): A controlled-release Galenical preparation of pharmaceutically acceptable form of Diltiazem including the pharmaceutically acceptable salts thereof, for evening dosing every 24 hours containing from about 120 mg to about 540 mg of the form of Diltiazem with excipients to provide controlled (sustained) release of the form of Diltiazem from the preparation for providing a Cmax of Diltiazem in the blood at between about 10 hours and about 15 hours (Tmax) after administration of the preparation, the preparation being in a sustained-release dosage form in which the form of Diltiazem is adapted to be control released after administration of the preparation over a period of time and being adapted to release the Diltiazem

(i) into an aqueous medium at the following rates measured using the method of United States Pharmacopoeia No. XXIII at 100 rpm in 900 ml of water:

- (a) between about 1% and about 15% after 2 hours;
- (b) between about 7% and about 35% after 4 hours;
- (c) between about 30% and about 58% after 8 hours;
- (d) between about 55% and about 80% after 14 hours; and
- (e) and in excess of about 75% after 24 hours.

and/or (ii) into a buffered medium having a pH between about 5.5 and about 6.5, at the following rates measured using the method of United States Pharmacopoeia No. XXIII at 100 rpm in 900ml of the buffered medium:

- (a) between about 1% and about 25% after about 2 hours;
- (b) between about 7% and about 45% after about 4 hours;
- (c) between about 30% and about 68% after about 8 hours;
- (d) in excess of about 75% after about 24 hours wherein the preparation comprises a plurality of microgranules, wherein each microgranule comprises a central core of the form of diltiazem or a pharmaceutically acceptable salt thereof,

associated with a wetting agent, wherein the central core is coated with a microporous membrane comprising at least one lubricant and/or at least one hydrophilic polymer and at least one water insoluble swellable polymer which permits hydration of the core by gastrointestinal fluids, and wherein the wetting agent is selected from the group consisting of:

sugars;  
saccharose, mannitol, sorbitol;  
lecithins;  
C<sub>12</sub> to C<sub>20</sub> fatty acid esters of saccarose,;  
xylose esters or xylites;  
polyoxyethylenic glycerides;  
esters of fatty acids and polyoxyethylene;  
sorbitan fatty acid esters;  
polyglycides-glycerides and polyglycides-alcohols esters and  
Metal salts.

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Claim 45 (previously amended): The preparation of claim 9 wherein the wetting agent is in association with the diltiazem in the microgranule and not mixed therewith, the membrane comprises a water-soluble or water dispersible polymer or copolymer and a water-, acid- and base-insoluble polymer which is a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester enabling the bead to be hydrated by the introduction of intestinal fluids into the core hydrating the core and therefore mixing the diltiazem and the wetting agent.

Claim 46 (previously amended): A method of treatment of a patient's hypertension and/or angina comprising the administration of the preparation of claim 44 to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning.

Claim 47 (previously amended): A method of treatment of a patient's hypertension and/or angina comprising the administration of the preparation of claim 3 to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning wherein each microgranule comprises a central core of the form of diltiazem or a pharmaceutically acceptable salt thereof, associated with a wetting agent, wherein the central core is coated with a microporous membrane and wherein the wetting agent is in association with the diltiazem in the microgranule and not mixed therewith, the membrane comprises a water-soluble or water dispersible polymer or copolymer and a water-, acid- and base-insoluble polymer which is a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester enabling the bead to be hydrated by the introduction of intestinal fluids into the core hydrating the core and therefore mixing the diltiazem and the wetting agent.

Claim 48 (previously amended): A controlled-release Galenical preparation of pharmaceutically acceptable form of Diltiazem including the pharmaceutically acceptable salts thereof, for evening dosing every 24 hours containing from about 120 mg to about 540 mg of the form of Diltiazem with excipients to provide controlled (sustained) release of the form of Diltiazem from the preparation for providing a Cmax of Diltiazem in the blood at between about 10 hours and about 15 hours (Tmax) after administration of the preparation, the preparation being in a sustained-release dosage form in which the Diltiazem is adapted to be control released after administration of the preparation over a period of time and being adapted to release the Diltiazem

(i) into an aqueous medium at the following rates measured using the method of United States Pharmacopoeia No. XXIII at 100 rpm in 900 ml of water:

- (a) between about 1% and about 15% after 2 hours;
- (b) between about 7% and about 35% after 4 hours;
- (c) between about 30% and about 58% after 8 hours;
- (d) between about 55% and about 80% after 14 hours; and
- (e) and in excess of about 75% after 24 hours.

and/or (ii) into a buffered medium having a pH between about 5.5 and about 6.5, at the following rates measured using the method of United States Pharmacopoeia No. XXIII at 100 rpm in 900ml of the buffered medium:

- (a) between about 1% and about 25% after about 2 hours;
- (b) between about 7% and about 45% after about 4 hours;
- (c) between about 30% and about 68% after about 8 hours;
- (d) in excess of about 75% after about 24 hours, wherein the preparation

comprises a plurality of microgranules, wherein each microgranule comprises a central core of the form of diltiazem or a pharmaceutically acceptable salt thereof, associated with a wetting agent, wherein the central core is coated with a microporous membrane in which the core and membrane comprise:

	% W/W
(a) Diltiazem hydrochloride	69 - 73
(b) Microcrystalline cellulose	8 - 9.5
(c) Povidone K30	1 - 2
(d) Sucrose stearate	7 - 8
(e) Magnesium stearate NF	0.5 - 2.5
(f) Talc USP	0.5 - 5.0
(g) Titanium dioxide (USP)	0.15 - 0.3
(h) Hydroxypropylmethylcellulose 2910	0.3 - 0.6
(i) Polysorbate 80 (tween)	0.01 - 0.025
(j) Simeticone C emulsion USP (dry of 30%)	0.01 - 0.015
(k) a neutral copolymer of acrylic acid ethyl ester and acrylic	

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cont.

acid methyl ester (dry of 30%)  
Purified water USP

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0 (used for mixing).

Claim 49 (previously amended): A method of treatment of a patient's hypertension and/or angina comprising the administration of the preparation of claim 48 to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning.

Claim 50 (currently amended): A controlled-release Galenical preparation of pharmaceutically acceptable form of Diltiazem including the pharmaceutically acceptable salts thereof, for evening dosing every 24 hours containing from about 120 mg to about 540 mg of the form of Diltiazem with excipients to provide controlled (sustained) release of the form of Diltiazem from the preparation for providing a Cmax of Diltiazem in the blood at between about 10 hours and about 15 hours (Tmax) after administration of the preparation, the preparation being in a sustained-release dosage form in which the Diltiazem is adapted to be control released after administration of the preparation over a period of time and being adapted to release the Diltiazem

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(i) into an aqueous medium at the following rates measured using the method of United States Pharmacopoeia No. XXIII at 100 rpm in 900 ml of water:

- (a) between about 1% and about 15% after 2 hours;
- (b) between about 7% and about 35% after 4 hours;
- (c) between about 30% and about 58% after 8 hours;
- (d) between about 55% and about 80% after 14 hours; and
- (e) and in excess of about 75% after 24 hours.

and/or (ii) into a buffered medium having a pH between about 5.5 and about 6.5, at the following rates measured using the method of United States Pharmacopoeia No. XXIII at 100 rpm in 900ml of the buffered medium:

- (a) between about 1% and about 25% after about 2 hours;
- (b) between about 7% and about 45% after about 4 hours;
- (c) between about 30% and about 68% after about 8 hours;
- (d) in excess of about 75% after about 24 hours, wherein the preparation

comprises a plurality of microgranules, wherein each microgranule comprises a central core of the form of diltiazem or a pharmaceutically acceptable salt thereof, associated with a wetting agent, wherein the central core is coated with a microporous membrane in which the core and membrane comprise:

- (i) in the core,

(a) between about 50% and about 85% (% w/w of the total preparation) of Diltiazem or pharmaceutically acceptable salt thereof; and

(b) between about 2% and about 25% wetting agent (% w/w of the total preparation);

together with adjuvants; and

(ii) in the membrane,

(c) between about 0.1% and about 50% of the total preparation of at least on lubricant, and/or

(d) ~~(e)~~ between about 0.1% and about 2% of the total preparation of water-soluble and/or water-dispersible polymer; and

(e) ~~(d)~~ between about 5% and about 20% (% w/w of the preparation) of a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester, together with adjuvants, which permits hydration of the core by gastrointestinal fluids.

Claim 51 (previously amended): A method of treatment of a patient's hypertension and/or angina comprising the administration of the preparation of claim 50 to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning.

Claim 52 (currently amended): A controlled-release Galenical preparation of pharmaceutically acceptable form of Diltiazem including the pharmaceutically acceptable salts thereof, for evening dosing every 24 hours containing from about 120 mg to about 540 mg of the form of Diltiazem with excipients to provide controlled (sustained) release of the form of Diltiazem from the preparation for providing a Cmax of Diltiazem in the blood at between about 10 hours and about 15 hours (Tmax) after administration of the preparation, the preparation being in a sustained-release dosage form in which the Diltiazem is adapted to be control released after administration of the preparation over a period of time and being adapted to release the Diltiazem

(i) into an aqueous medium at the following rates measured using the method of United States Pharmacopoeia No. XXIII at 100 rpm in 900 ml of water:

- (a) between about 1% and about 15% after 2 hours;
- (b) between about 7% and about 35% after 4 hours;
- (c) between about 30% and about 58% after 8 hours;

- (d) between about 55% and about 80% after 14 hours; and
- (e) and in excess of about 75% after 24 hours.

and/or (ii) into a buffered medium having a pH between about 5.5 and about 6.5, at the following rates measured using the method of United States Pharmacopoeia No. XXIII at 100 rpm in 900ml of the buffered medium:

- (a) between about 1% and about 25% after about 2 hours;
- (b) between about 7% and about 45% after about 4 hours;
- (c) between about 30% and about 68% after about 8 hours;
- (d) in excess of about 75% after about 24 hours, wherein the preparation comprises a plurality of microgranules, wherein each microgranule comprises a central core of the form of diltiazem or a pharmaceutically acceptable salt thereof, associated with a wetting agent, wherein the central core is coated with a microporous membrane in which the core and membrane comprise:

- (i) in the core,

(a) between about 69% and about 73% (% w/w of the total preparation) of Diltiazem or pharmaceutically acceptable salt thereof; and

(b) between about 7% and about 8% wetting agent (% w/w of the total preparation);

together with adjuvants; and

- (ii) in the membrane,

(c) between about 0.1% and about 50% of the total preparation of at least one lubricant, and/or

(d) (e) between about 0.3% and about 0.6% of the total preparation of water-soluble and/or water-dispersible polymer; and

(e) (d) between about 7% and about 11% (% w/w of the preparation) of a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester, together with adjuvants, which permits hydration of the core by gastrointestinal fluids.

Claim 53 (previously amended): A method of treatment of a patient's hypertension and/or angina comprising the administration of the preparation of claim 52 to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning.



Claim 54 (previously amended): The preparation of claim 9, 10, 11, 12, 13, 14, 15, 16, 44 or 45 wherein the preparation is a tablet and the tablet comprises microgranules in association with wax placebo beads which wax placebo beads serve to absorb the shock placed on the microgranules of Diltiazem during the tablet process, together with excipients and adjuvants.

Claim 55 (previously amended): A method of treatment of a patient's hypertension and/or angina comprising the administration of the preparation of claim 54 to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning.

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Claim 56 (currently amended): A controlled-release Galenical preparation of pharmaceutically acceptable form of Diltiazem including the pharmaceutically acceptable salts thereof, for evening dosing every 24 hours containing from about 120 mg to about 540 mg of the form of Diltiazem with excipients to provide controlled (sustained) release of the form of Diltiazem from the preparation for providing a Cmax of Diltiazem in the blood at between about 10 hours and about 15 hours (Tmax) after administration of the preparation, the preparation being in a sustained-release dosage form in which the Diltiazem is adapted to be control released after administration of the preparation over a period of time wherein the preparation comprises a plurality of microgranules, each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent in which the core and membrane comprise:

- (i) in the core,
  - (a) between about 50% and about 85% (% w/w of the total preparation) of Diltiazem or pharmaceutically acceptable salt thereof; and
  - (b) between about 2% and about 25% wetting agent (% w/w of the total preparation);

together with adjuvants; and

- (ii) in the membrane,
  - (c) between about 0.1% and about 50% of the total preparation of at least one lubricant, and/or

~~(d)~~ ~~(e)~~ between about 0.1% and about 2% of the total preparation of water-soluble and/or water-dispersible polymer; and

~~(e)~~ ~~(d)~~ between about 5% and about 20% (% w/w of the preparation) of a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester, together with adjuvants, which permits hydration of the core by gastrointestinal fluids.

Claim 57 (original): The preparation of claim 56 wherein the microgranules are in capsule form.

Claim 58 (original): The preparation of claim 56 wherein the microgranules are in tablet form.

Claim 59 (currently amended): The preparation of claim 56, 57 or 58 wherein the core and membrane comprise:

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(i) in the core,

(a) between about 69% and about 73% (% w/w of the total preparation) of Diltiazem or pharmaceutically acceptable salt thereof; and

(b) between about 7% and about 8% wetting agent (% w/w of the total preparation);

together with adjuvants; and

(ii) in the membrane,

(c) between about 0.1% and about 50% of the total preparation of at least one lubricant, and/or

~~(d)~~ ~~(e)~~ between about 0.3% and about 0.6% of the total preparation of water-soluble and/or water-dispersible polymer; and

~~(e)~~ ~~(d)~~ between about 7% and about 11% (% w/w of the preparation) of a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester, together with adjuvants.

Claim 60 (previously amended): A controlled-release Galenical preparation of pharmaceutically acceptable form of Diltiazem including the pharmaceutically acceptable salts thereof, for evening dosing every 24 hours containing from about

120 mg to about 540 mg of the form of Diltiazem with excipients to provide controlled (sustained) release of the form of Diltiazem from the preparation for providing a Cmax of Diltiazem in the blood at between about 10 hours and about 15 hours (Tmax) after administration of the preparation, the preparation being in a sustained-release dosage form in which the Diltiazem is adapted to be control released after administration of the preparation over a period of time wherein the preparation comprises a plurality of microgranules, each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent in which the core and membrane comprise:

(i) in the core,

(a) between about 50% and about 85% (% w/w of the total preparation) of Diltiazem or pharmaceutically acceptable salt thereof; and

(b) between about 2% and about 25% wetting agent (% w/w of the total preparation);

together with adjuvants; and

(ii) in the membrane,

(c) between about 0.1% and about 2% of the total preparation of water-soluble and/or water-dispersible polymer; and

(d) between about 5% and about 20% (% w/w of the preparation) of a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester, together with adjuvants wherein the core and membrane comprise:

	% W/W
(a) Diltiazem hydrochloride	69 - 73
(b) Microcrystalline cellulose (Avicel ph101)	8 - 9.5
(c) Povidone K30	1 - 2
(d) Sucrose stearate (crodesta F150)	7 - 8
(e) Magnesium stearate NF	0.5 - 2.5
(f) Talc USP	0.5 - 5.0
(g) Titanium dioxide (USP)	0.15 - 0.3
(h) Hydroxypropylmethylcellulose 2910	0.3 - 0.6
(i) Polysorbate 80 (tween)	0.01 - 0.025
(j) Simeticone C emulsion USP (dry of 30%)	0.01 - 0.015
(k) a neutral copolymer of acrylic acid ethyl ester and acrylic	

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cont.

acid methyl ester (dry of 30%)  
Purified water USP

7 - 11  
0 (used for mixing).

Claim 61 (previously amended): The preparation of claim 56, 58, 59 or 60 wherein the preparation is a tablet and the tablet comprises microgranules in association with wax placebo beads which wax placebo beads serve to absorb the shock placed on the microgranules of Diltiazem during the tablet process, together with excipients and adjuvants.

Claim 62 (previously amended): A method of treatment of a patient's hypertension and/or angina comprising the administration of the preparation of claim 56 to the patient in the evening for effective treatment of the patient's hypertension and/or angina the next morning.

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Claim 63 (previously added): The preparation of claim 1, 2, 3 or 4 in capsule form wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises a form of Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent.

Claim 64 (previously added): The preparation of claim 1, 2, 3 or 4 in capsule form, wherein the preparation releases the Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution, and wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent.

Claim 65 (previously added): The preparation of claim 1, 2, 3 or 4 in tablet form wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of Diltiazem coated with a microporous membrane and the central core comprises a form of Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent.

Claim 66 (previously added): The preparation of claim 1, 2, 3 or 4 in tablet form wherein the preparation releases the Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution, and wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of Diltiazem coated with a microporous membrane and the central core comprises a form of Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent.

Claim 67 (previously added): The preparation of claim 1, 2, 3 or 4 in capsule form wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of Diltiazem coated with a microporous membrane and the central core comprises a form of Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent, wherein the Diltiazem is mixed (in whole or in part) with the wetting agent.

Claim 68 (previously added): The preparation of claim 1, 2, 3 or 4 in capsule form, wherein the preparation releases the Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution, and wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the Diltiazem is mixed (in whole or in part) with the wetting agent.

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Claim 69 (previously added): The preparation of claim 1, 2, 3 or 4 in tablet form wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent wherein the Diltiazem is mixed (in whole or in part) with the wetting agent.

Claim 70 (previously added): The preparation of claim 1, 2, 3 or 4 in tablet form wherein the preparation releases the Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution, and wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the Diltiazem is mixed (in whole or in part) with the wetting agent.

Claim 71 (previously added): The preparation of claim 1, 2, 3 or 4 in capsule form wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent, wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein.

Claim 72 (previously added): The preparation of claim 1, 2, 3 or 4 in capsule form, wherein the preparation releases the Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution, and wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein.

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Claim 73 (previously added): The preparation of claim 1, 2, 3 or 4 in tablet form wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein.

Claim 74 (previously added): The preparation of claim 1, 2, 3 or 4 in tablet form wherein the preparation releases the Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution, and wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein.

Claim 75 (previously added): The preparation of claim 1, 2, 3 or 4 in capsule form wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent, wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet

therein wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation.

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Claim 76 (previously added): The preparation of claim 1, 2, 3 or 4 in capsule form, wherein the preparation releases the Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution, and wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation.

Claim 77 (previously added): The preparation of claim 1, 2, 3 or 4 in tablet form wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation.

Claim 78 (previously added): The preparation of claim 1, 2, 3 or 4 in tablet form wherein the preparation releases the Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution, and wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem

is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation.

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Claim 79 (previously added): The preparation of claim 1, 2, 3 or 4 in capsule form wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent, wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose.

Claim 80 (previously added): The preparation of claim 1, 2, 3 or 4 in capsule form, wherein the preparation releases the Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution, and wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose.

Claim 81 (previously added): The preparation of claim 1, 2, 3 or 4 in tablet form wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting



agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose.

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cont. - Claim 82 (previously added): The preparation of claim 1, 2, 3 or 4 in tablet form wherein the preparation a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose.

Claim 83 (previously added): The preparation of claim 1, 2, 3 or 4 in capsule form wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent, wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside).

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Claim 84 (previously added): The preparation of claim 1, 2, 3 or 4 in capsule form, wherein the preparation releases the Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution, and wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside).

Claim 85 (previously added): The preparation of claim 1, 2, 3 or 4 in tablet form wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside).

Claim 86 (previously added): The preparation of claim 1, 2, 3 or 4 in tablet form wherein the preparation releases the Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution, and wherein the preparation is a

diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside).

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Claim 87 (previously added): The preparation of claim 1, 2, 3 or 4 in capsule form wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent, wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside) wherein the preparation contains 120 mg of Diltiazem.

Claim 88 (previously added): The preparation of claim 1, 2, 3 or 4 in capsule form, wherein the preparation releases the Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution, and wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane

and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside) wherein the preparation contains 120 mg of Diltiazem.

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Claim 89 (previously added): The preparation of claim 1, 2, 3 or 4 in tablet form wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside) wherein the preparation contains 120 mg of Diltiazem.

Claim 90 (previously added): The preparation of claim 1, 2, 3 or 4 in tablet form wherein the preparation releases the Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution, and wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the Diltiazem is mixed (in whole or in

part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside) wherein the preparation contains 120 mg of Diltiazem.

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Claim 91 (previously added): The preparation of claim 1, 2, 3 or 4 in capsule form wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent, wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside) wherein the preparation contains 180 mg of Diltiazem.

Claim 92 (previously added): The preparation of claim 1, 2, 3 or 4 in capsule form, wherein the preparation releases the Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution, and wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem

is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside) wherein the preparation contains 180 mg of Diltiazem.

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Claim 93 (previously added): The preparation of claim 1, 2, 3 or 4 in tablet form wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the Diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside) wherein the preparation contains 180 mg of Diltiazem.

Claim 94 (previously added): The preparation of claim 1, 2, 3 or 4 in tablet form wherein the preparation releases the Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution, and wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of Diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a

water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside) wherein the preparation contains 180 mg of Diltiazem.

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Claim 95 (previously added): The preparation of claim 1, 2, 3 or 4 in capsule form wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent, wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside) wherein the preparation contains 240 mg of Diltiazem.

Claim 96 (previously added): The preparation of claim 1, 2, 3 or 4 in capsule form, wherein the preparation releases the Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution, and wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid

ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside) wherein the preparation contains 240 mg of Diltiazem.

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Claim 97 (previously added): The preparation of claim 1, 2, 3 or 4 in tablet form wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside) wherein the preparation contains 240 mg of Diltiazem.

Claim 98 (previously added): The preparation of claim 1, 2, 3 or 4 in tablet form wherein the preparation releases the Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution, and wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the



membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside) wherein the preparation contains 240 mg of Diltiazem.

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Claim 99 (previously added): The preparation of claim 1, 2, 3 or 4 in capsule form wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent, wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside) wherein the preparation contains 300 mg of Diltiazem.

Claim 100 (previously added): The preparation of claim 1, 2, 3 or 4 in capsule form, wherein the preparation releases the Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution, and wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and

hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside) wherein the preparation contains 300 mg of Diltiazem.

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Claim 101 (previously added): The preparation of claim 1, 2, 3 or 4 in tablet form wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside) wherein the preparation contains 300 mg of Diltiazem.

Claim 102 (previously added): The preparation of claim 1, 2, 3 or 4 in tablet form wherein the preparation releases the Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution, and wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a

concentration gradient through the membrane (high concentration inside and low concentration outside) wherein the preparation contains 300 mg of Diltiazem.

Claim 103 (previously added): The preparation of claim 1, 2, 3 or 4 in capsule form wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent, wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside) wherein the preparation contains 360 mg of Diltiazem.

Claim 104 (previously added): The preparation of claim 1, 2, 3 or 4 in capsule form, wherein the preparation releases the Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution, and wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside) wherein the preparation contains 360 mg of Diltiazem.

Claim 105 (previously added): The preparation of claim 1, 2, 3 or 4 in tablet form wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside) wherein the preparation contains 360 mg of Diltiazem.

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Claim 106 (previously added): The preparation of claim 1, 2, 3 or 4 in tablet form wherein the preparation releases the Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution, and wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside) wherein the preparation contains 360 mg of Diltiazem.

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Claim 107 (previously added): The preparation of claim 1, 2, 3 or 4 in capsule form wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent, wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside) wherein the preparation contains 420 mg of Diltiazem.

Claim 108 (previously added): The preparation of claim 1, 2, 3 or 4 in capsule form, wherein the preparation releases the Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution, and wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside) wherein the preparation contains 420 mg of Diltiazem.

Claim 109 (previously added): The preparation of claim 1, 2, 3 or 4 in tablet form wherein the preparation is a diffusion controlled preparation and wherein each

microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside) wherein the preparation contains 420 mg of Diltiazem.

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Claim 110 (previously added): The preparation of claim 1, 2, 3 or 4 in tablet form wherein the preparation releases the Diltiazem at a rate of less than about 15% of the total amount of active per hour during dissolution, and wherein the preparation is a diffusion controlled preparation and wherein each microgranule comprising a central core containing the form of diltiazem coated with a microporous membrane and the central core comprises Diltiazem or pharmaceutically acceptable salt thereof associated with a wetting agent and wherein the Diltiazem is mixed (in whole or in part) with the wetting agent wherein the wetting agent assists to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein and wherein the membrane comprises a water-dispersible or water-soluble polymer and a water-, acid- and base-insoluble polymer of a neutral acrylic polymer including a neutral copolymer of acrylic acid ethyl ester and acrylic acid methyl ester which hydrates the preparation wherein the membrane further comprises hydroxypropylmethylcellulose and wherein the membrane hydrates the core within the membrane which when put in gastrointestinal fluid causes the membrane to swell while fluid penetrates and hydrates the bead, and dissolves the diltiazem and wetting agent and benefits from a concentration gradient through the membrane (high concentration inside and low concentration outside) wherein the preparation contains 420 mg of Diltiazem.

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